#### From the INTERNATIONAL SEARCHING AUTHORITY To: RONALD W. CITKOWSKI GIFFORD, KRASS, GROH, SPRINKLE, ANDERSON & CITKOWSKI, P.C. WRITTEN OPINION OF THE 280 N. OLD WOODWARD AVE., STE. 400 INTERNATIONAL SEARCHING AUTHORITY BIRMINGHAM, MI 48009 (PCT Rule 43bis.1) Date of mailing (day/month/year) Applicant's or agent's file reference FOR FURTHER A See paragraph 2 below NEN-22452/16 International application No. International filing date (day/month/year) Priority date (day/month/year) PCT/US04/21639 02 July 2004 (02.07.2004) 02 July 2003 (02.07.2003) International Patent Classification (IPC) or both national classification and IPC IPC(7): G01N 23/00, 21/76 and US Cl.: 436/56, 57, 172, 800; 250/483.1, 486.1, 302, 303 Applicant PERKINELMER LAS, INC. 1. This opinion contains indications relating to the following items: Box No. I Basis of the opinion Box No. II Priority Non-establishment of opinion with regard to novelty, inventive step and industrial applicability Box No. III Box No. IV Lack of unity of invention Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial Box No. V applicability; citations and explanations supporting such statement Box No. VI Certain documents cited Certain defects in the international application Box No. VII Box No. VIII Certain observations on the international application 2. FURTHER ACTION If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1 bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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Commissioner for Patents

P.O. Box 1450

Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Jill Warden

Telephone No. 571-272-1700

Form PCT/ISA/237 (cover sheet) (January 2004)

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

international application ivo.

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Box No. 1 Basis of this opinion				
1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.				
This opinion has been established on the basis of a translation from the original language into the following language which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).				
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:				
a. type of material				
a sequence listing				
table(s) related to the sequence listing				
b. format of material				
in written format				
in computer readable form				
c. time of filing/furnishing				
contained in international application as filed.				
filed together with the international application in computer readable form.				
furnished subsequently to this Authority for the purposes of search.				
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In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.				
4. Additional comments:				

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Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement		
1. Statement		
Novelty (N)	Claims 13, 25-27	YES
crovers (cry	Claims 1-12, 14-24	
Inventive step (IS)	Claims NONE	YES
inventive step (15)	Claims <u>1-27</u>	
Industrial applicability (IA)	Claims 1-27	YES
musurar applicationity (21)	Claims NONE	
2. Citations and explanations:		
Please See Continuation Sheet		
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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

V. 2. Citations and Explanations:

Claims 1-4 and 8 lack novelty under PCT Article 33(2) as being anticipated by Franks et al.

Franks et al teach of a liquid scintillator composition comprising Coumarin 540-A (also known as Coumarin-153) in a suitable solvent such as benzyl alcohol. In example III of Franks et al, a liquid scintllator composition containing both Coumarin 540-A and BiBuQ (4, 4"-Di 2 butyloctoxyl-1)-P-quaterphenyl) is taught. Coumarin 540-A has a Stokes shift of at least 100 nm, and a fluorescent emission in the range of 460-500 nm. See column 2, lines 45-60, column 5, lines 44-48 and column 6, lines 1-26 of Franks et al.

Claims 1-6, 9-12 and 14-22 lack novelty under PCT Article 33(2) as being anticipated by Lerner et al.

Lerner et al teach of fluorescent latex particles having at least one hydrophobic fluorochrome A and at least one hydrophobic fluorochrome D encapsulated therein. Lerner et al teach that the two fluorochromes can be 9, 10 diphenyl-anthracene (9,10 DPA) and Coumarin 153. See column 2, lines 15-64 and column 3, lines 20 and 33-39 of Lerner et al. The fluorochromes are encapsulated in solid, polymeric particles. Lerner et al teach that the solid particles can be used in biological analyses such as rountine scintillation assays. See column 5, lines 8-21 and claims 5, 6 and 16 in Lerner et al. Coumarin 540-A has a Stokes shift of at least 100 nm, and a fluorescent emission in the range of 460-500 nm.

Claims 1-4, 6-7, 16-21 and 23-24 lack novelty under PCT Article 33(2) as being anticipated by Kessler et al.

Kessler et al teach of a composition containing a solid polyacrylamide gel doped with one or more laser dyes to provide fluorescence at a plurality of wavelengths. Kessler et al teach that the one or more laser dyes can include BiBuQ and Coumarin 153. See column 1, lines 40-56, column 2, lines 45-67, column 3, lines 1-12 and claims 17 and 21 of Kessler et al. Coumarin 153 has a Stokes shift of at least 100 nm, and a fluorescent emission in the range of 460-500 nm.

Claim 13 lacks an inventive step under PCT Article 33(3) as being obvious over Lerner et al. For a teaching of Lerner et al, see previous paragraphs.

Lerner et al fail to teach that the combination of the Coumarin 153 and 9,10 DPA can be present in a liquid composition. However, it would have been obvious to one of ordinary skill in the art to use the Coumarin 153 and 9,10 DPA fluorochromes taught by Lerner et al in a liquid scintillator composition since the "Background of the Invention" portion of the disclosure admits that it is well known in the art to incorporate flourochrome materials such as 9,10 DPA into liquid scintillator compositions.

Claims 25-27 lack an inventive step under PCT Article 33(3) as being obvious over Thomson et al in view of Frnaks et al. For a teaching of Franks et al, see previous paragraphs.

Thomson et al teach of a liquid scintillation composition comprising a solvent and a fluor system. Thomson et al teach that the fluor system can include one or more dyes such as 2, 5-diphenyloxazole (PPO) and 1,4-di-(2-methylstyryl) benzene (bis-MSB). See column 1, lines 50-61 and column 4, lines 11-21 of Thomson et al. Thomson et al fail to teach that the fluor system can include a Coumarin dye therein.

Based upon the combination of Thomson et al and Franks et al, it would have been obvious to one of ordinary skill in the art to

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	include a Coumarin dye in the liquid scintillation composition taught by Thomson et al since Franks et al teach that it is known in the art to use Coumarin dyes as fluorescent scintillators in liquid compositions, and Thomson et al teach of using more than one fluorescent dye material in the fluor system of the liquid scintillation composition.	
	Claims 1-27 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.	
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